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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	5

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/234,733	Jiang et al
Examiner	**Group Art Unit**
Li Lee	1645

Responsive to communication(s) filed on _____.

This action is **FINAL.**

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

X Claim(s) 1-12 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

Claim(s) _____ is/are allowed.

X Claim(s) 1-12 is/are rejected.

Claim(s) _____ is/are objected to.

Claims _____ are subject to restriction or election requirement.

Application Papers

X See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

X Notice of References Cited, PTO-892

X Information Disclosure Statement(s), PTO-1449, Paper No(s). 2

Interview Summary, PTO-413

SEE OFFICE ACTION ON THE FOLLOWING PAGES

DETAILED ACTION

Drawings

1. This application has been filed with informal drawings which are acceptable for examination purposes only. The drawings are objected to by the draftsperson under 37 C.F.R. 1.84 or 1.152. See PTO-948 for details. Correction of the noted defects can be deferred until the application is allowed by the examiner.

Information Disclosure Statement

2. Items listed on form PTO-1449 have be considered by the examiner.

Claim Rejections - 35 USC § 112

3 The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention

4. Claims 2-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

5. Claims 2-3 are indefinite for leaving the SEQ ID NO blank in claim 2, line 12 and claim 3, line 19. Without reciting a specific SEQ ID NO the metes and bounds of the claims cannot be determined. Claims 2-3 are further indefinite for using the term "substantially homologous" which has no clearly defined meaning as applied to a amino acid sequence. The term substantially homologous in the claims is a relative term which renders the claim indefinite, in the absence of a clear recitation of the specific algorithm and specific parameters employed for comparison of sequences. The term substantially homologous in the specification does not provide a standard for ascertaining the requisite degree, and one of the ordinary skill in the art would not be reasonably be apprised of the metes and bounds of the claimed subject matter. Claims 2-3 are further indefinite for using the term "functionally equivalent" which has no clearly defined meaning as applied to a amino acid sequence. It is not clear what the characteristics and properties of the functionally equivalent are.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-3, 5-6, 8-9, and 11-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a isolated nucleic acid molecule encoding the amino enablement for any variant of a isolated nucleic acid molecule encoding the amino acid sequence

of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 2-3, 5-6, 8-9, and 11-12 are drawn to and encompass a isolated nucleic acid molecule encoding a polypeptide variant which has a substantially homologous and functionally equivalent to the amino acid sequence of SEQ ID NO:2. The claims are not enabled for the reasons set forth below. The specification fails to recite the specifically algorithm and parameters used to determine the homologous of the claimed invention. The outcome of the comparison is certainly dependent on how the sequences are compared (George et al. Macromol Sequencing Synthesis, Select Meth Appl, pages 127-149, 1988 Alan Liss, Inc.). The specification fails to provide characteristics of any polypeptide variants of the SEQ ID NO:2 which function as a *Streptococcus uberis* CAMP factor polypeptide equivalent to the disclosed SEQ ID NO:2. The specification fails to teach the biological functionally equivalent of the protein. One skilled in the art would have reason to doubt the alleged function of the protein because the art teaches that polypeptide isolated based on percent homology do not predictably display the functions of their homologs (Herzog et al., DNA and Cell Biology, 12(6):465-471, 1993, see abstract). The specification fails to teach what are the critical protein portions that are needed for the

unpredictable areas of biotechnology and the art teaches that the significance [illegible]

amino acid and sequences for different aspects of biological activity can not be predicted a *priori* and must be determined empirically on a case by case basis (Rudinger et al., in "Peptide Hormones", edited by Parsons, J.A., University Park Press, June 1976, page 6). The art specifically teaches that even a single amino acid change in a protein leads to unpredictable change in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). Moreover, no assay for *Streptococcus uberis* CAMP factor homolog function is set forth in the specification which could allow one skilled in the art to screen for functionally equivalent variants. In view of the lack of any guidance of any protein variant that functions equivalently to the protein of SEQ ID NO:2, the lack of an enabling description of how to obtain and make and use a isolated nucleic acid molecule encoding the amino acid variants of SEQ ID NO:2, the unpredictability associated with making and using a isolated nucleic acid molecule encoding the variants of SEQ ID NO:2 encompassed in the scope of the claims as set forth above, the lack of teaching even a beginning point for variation of the variant of the protein sequence of SEQ ID NO:2 for routine experimentation, the lack of an assay to screen for variants, the skilled artisan would be forced into undue experimentation to practice

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Williams et al. (Lett Appl Microbiol 12(1):23-8, 1991).

Claims 1-3 are drawn and encompass to an isolated nucleic acid molecule comprising a coding sequence encodes an amino acid sequence for an immunogenic *Streptococcus uberis* CAMP factor and substantially homologous and functionally equivalent to the amino acid sequence shown in Figures 4A-4C or an immunogenic fragment thereof.

Williams et al. teach an isolated chromosomal DNA from *Streptococcus uberis* which inherently comprises the coding sequence encoding *Streptococcus uberis* CAMP factor, thus Williams et al meet the limitations of the claims.

9. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Podblielski (Med Microbiol Immunol 183:239-256, 1994).

coding sequence encodes an amino acid sequence for an immunogenic *Streptococcus uberis*

CAMP factor and substantially homologous and functionally equivalent to the amino acid sequence shown in Figures 4A-4C or an immunogenic fragment thereof.

Podblielski teaches an isolated nucleic acid molecule of the cf6 gene encoding group B *Streptococcus* CAMP factor comprising a coding sequence encodes an amino acid sequence for an immunogenic *Streptococcus uberis* CAMP factor (e.g., identical epitopes, see the sequence search from database SPTREMBL, result 2) and substantially homologous (having 63.5 % Query Match, see the sequence search from database SPTREMBL, result 2) and functionally equivalent (e.g., there are 10 epitopes in the query sequence identical to SEQ ID NO:2, see the sequence search from database SPTREMBL, result 2) to the amino acid sequence shown in Figures 4A-4C of SEQ ID NO:2 and an immunogenic fragment (e.g., epitope) thereof. Because the art teaches that an immunogenic fragment (an immunogenic epitope) is approximately equivalent to 5 amino acids (Levinson et al. Examination & Board Review, Medical Microbiology & Immunology, page 293, 1994) and there are 10 epitopes in the group B *Streptococcus* CAMP factor sequence identical to SEQ ID NO:2, thus Podblielski meets the limitations of the claims.

Claim Rejections - 35 USC § 103

Objections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Podblielski (Med Microbiol Immunol 183:239-256, 1994) applied to claims 1-3 and Sambrook et al. (Molecular Cloning, A Laboratory Manual CSH 1989, 17 Expression of Cloned Genes in *Escherichia coli*).

Podblielski teaches a cloned nucleic acid molecule comprising a coding sequence encodes an amino acid sequence for an immunogenic *Streptococcus uberis* CAMP factor and substantially homologous and functionally equivalent to the amino acid sequence shown in Figures 4A-4C or an immunogenic fragment thereof.

Podblielski does not teach inserting the cloned gene in to an expression vector comprising a heterologous control elements that are operably linked a DNA sequence which can be transcribed and translated in a host cell.

However, Sambrook et al. teach a standard method for expression of cloned genes (see pages 17.2-17.44, especially pages 17.3-17.4) including inserting a gene into a recombinant vector comprising a heterologous control elements that are operably linked a DNA sequence which can be transcribed and translated in a host cell.

at the time the invention was made to insert the cloned gene of Podblielski into a recombinant

vector comprising a heterologous control elements that can be operably linked the cloned sequence which can be transcribed and translated in a host cell due to the established advantages of gene cloning technic and provision for an unlimited supply of reagent.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Status of Claims

12. No claims are allowed. All claims stand rejected.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1645 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Lee, M.D., Ph.D. whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995.

Li Lee, M.D., Ph.D.
August 12, 1999

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